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USPT,PGPB,JPAB,EPAB,DWPI	cce and embryo$ and (teratogen$ or toxic$)	25	L22
USPT,PGPB,JPAB,EPAB,DWPI	cce and (teratogen$ or toxic$) and embryo$	25	L21
USPT,PGPB,JPAB,EPAB,DWPI	l19 and (toxic$ or teratogen$)	197	L20
USPT,PGPB,JPAB,EPAB,DWPI	l15 and l18	197	L19
USPT,PGPB,JPAB,EPAB,DWPI	l15 and (embryonic adj stem adj cell$1)	197	L18
USPT,PGPB,JPAB,EPAB,DWPI	l15 and (embryoid adj bod$)	0	L17
USPT,PGPB,JPAB,EPAB,DWPI	l15 and (embryo$ or stem or primordial)	1082	L16
USPT,PGPB,JPAB,EPAB,DWPI	l14 and (teratogen$ or toxic$)	2001	L15
USPT,PGPB,JPAB,EPAB,DWPI	protein and l5 and (immunoassay$ or immunodetect$)	5800	L14
USPT,PGPB,JPAB,EPAB,DWPI	protein and l5 and (immunoassay$)	5625	L13
USPT,PGPB,JPAB,EPAB,DWPI	protein and l5 and (mass adj spec$)	50	L12
USPT,PGPB,JPAB,EPAB,DWPI	l6 and (mass adj spec$)	3	L11
USPT,PGPB,JPAB,EPAB,DWPI	l5 and (mass adj spec$)	52	L10
USPT,PGPB,JPAB,EPAB,DWPI	l8 and (mass adj spec$)	1	L9
USPT,PGPB,JPAB,EPAB,DWPI	l7 and (protein$1 near5 expression)	892	L8
USPT,PGPB,JPAB,EPAB,DWPI	l6 and (toxic$ or teratogen$)	1090	L7
USPT,PGPB,JPAB,EPAB,DWPI	l5 and (embryoid or embryonic or primordial)	2183	L6
USPT,PGPB,JPAB,EPAB,DWPI	((435/4 |435/6 |435/7.1 |435/7.5 |435/7.6 |435/7.7 |435/7.72 |435/7.8 |435/7.9 |435/7.92 |435/325)!.CCLS.)	21228	L5
USPT,PGPB,JPAB,EPAB,DWPI	l2 and embryo$	25	L4
USPT,PGPB,JPAB,EPAB,DWPI	l1 same (toxic$ or teratogen$)	3	L3
USPT,PGPB,JPAB,EPAB,DWPI	l1 and (toxic$ or teratogen$)	48	L2
USPT,PGPB,JPAB,EPAB,DWPI	cce	477	L1

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Search History

Today's Date: 7/13/2001

DB Name	Query	Hit Count	Set Name
USPT,PGPB,JPAB,EPAB,DWPI	(embryoid adj bod$3).clm.	8	L9
USPT,PGPB,JPAB,EPAB,DWPI	primate.clm. and l3	1	L8
USPT,PGPB,JPAB,EPAB,DWPI	l6 and l3	0	L7
USPT,PGPB,JPAB,EPAB,DWPI	ovine.clm.	222	L6
USPT,PGPB,JPAB,EPAB,DWPI	l3 and l4	0	L5
USPT,PGPB,JPAB,EPAB,DWPI	(canine or goat or porcine or pig).clm.	3053	L4
USPT,PGPB,JPAB,EPAB,DWPI	(embryonic adj stem).clm.	128	L3
USPT,PGPB,JPAB,EPAB,DWPI	l1 same (canine or goat or porcine)	125	L2
USPT,PGPB,JPAB,EPAB,DWPI	embryonic adj stem	1713	L1

L5 ANSWER 14 OF 19 MEDLINE
AN 92209922 MEDLINE
DN 92209922 PubMed ID: 1725163
TI Pluripotent mouse embryonic stem cells are able to differentiate into cardiomyocytes expressing chronotropic responses to adrenergic and cholinergic agents and Ca2+ channel blockers.
AU Wobus A M; Wallukat G; Hescheler J
CS Institut fur Genetik und Kulturpflanzenforschung, Gatersleben, FRG.
SO DIFFERENTIATION, (1991 Dec) 48 (3) 173-82.
Journal code: E99; 0401650. ISSN: 0301-4681.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199205
ED Entered STN: 19920515
Last Updated on STN: 19960129
Entered Medline: 19920504
AB A defined cultivation system was developed for the differentiation of pluripotent embryonic stem cells of the mouse into spontaneously beating cardiomyocytes, allowing investigations of chronotropic responses, as well as electrophysiological studies of different cardioactive drugs in vitro. The beta-adrenoceptor agonists (-)isoprenaline and clenbuterol, the mediators of cAMP metabolism, forskolin and isobutylmethylxanthine (IBMX), the alpha 1-adrenoceptor agonist (-)phenylephrine, and the heart glycoside digitoxin induced a positive, the muscarinic cholinoceptor agonist carbachol and L-type Ca2+ channel blockers nisoldipine, gallopamil and diltiazem induced a negative chronotropic response. In early differentiated cardiomyocytes beta 1-, alpha 1-, but not beta 2-adrenoceptors, cholinoceptors, as well as L-type Ca2+ channels participated in the chronotropic response. In terminally differentiated cardiomyocytes beta 2-adrenoceptors and digitoxin responses were also functionally expressed. The contractions of spontaneously beating cardiomyocytes were concomitant with rhythmic action potentials very similar to those described for embryonic cardiomyocytes and sinus-node cells. We conclude that cardiomyocytes differentiating from pluripotent embryonic stem cells are able to develop adrenoceptors and cholinoceptors and signal transduction pathways as well as L-type Ca2+ channels as a consequence of cell-cell interactions during **embryoid body** formation in vitro, independent of the development in living organisms. The cellular system described may be useful as in vitro **assay** for toxicological investigations of chronotropic drugs and a model system for studying commitment and cellular differentiation in vitro.

Adonis

L24 ANSWER 14 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:120196 BIOSIS
DN PREV200000120196
TI Pharmacogenomics of the cystic fibrosis transmembrane conductance regulator (CFTR) and the cystic fibrosis **drug** CPX using genome microarray analysis.
AU Srivastava, Meera; Eidelman, Ofer; Pollard, Harvey B. (1)
CS (1) Department of Anatomy and Cell Biology, USU School of Medicine, USUHS, 4301 Jones Bridge Road, Bethesda, MD, 20814 USA
SO Molecular Medicine (New York), (Nov., 1999) Vol. 5, No. 11, pp. 753-767. ISSN: 1076-1551.
DT Article
LA English
SL English
AB Background: Cystic fibrosis (CF) is the most common lethal recessive disease affecting children in the U.S. and Europe. For this reason, a number of ongoing attempts are being made to treat the disease either by gene therapy or pharmacotherapy. Several phase 1 gene therapy trials have been completed, and a phase 2 clinical trial with the xanthine **drug** CPX is in progress. The protein coded by the principal CFTR mutation, DELTAF508-CFTR, fails to traffic efficiently from the endoplasmic reticulum to the plasma membrane, and is the pathogenic basis for the missing cAMP-activated plasma membrane chloride channel. CPX acts by binding to the mutant DELTAF508-CFTR and correcting the trafficking deficit. CPX also activates mutant CFTR channels. The comparative genomics of wild-type and mutant CFTR has not previously been studied. However, we have hypothesized that the **gene expression** patterns of human cells expressing mutant or wild-type CFTR might differ, and that a **drug** such as CPX might convert the mutant **gene expression** pattern into one more characteristic of wild-type CFTR. To the extent that this is true, a pharmacogenomic **profile** for such corrective **drugs** might be deduced that could simplify the process of **drug** discovery for CF. Materials and Methods: To **test** this hypothesis we used cDNA microarrays to study global **gene expression** in human cells permanently transfected with either wild-type or mutant CFTR. We also **tested** the effects of CPX on global **gene expression** when incubated with cells expressing either mutant or wild-type CFTR. Results: Wild-type and mutant DELTAF508-CFTR induce distinct and differential changes in cDNA microarrays, significantly affecting up to 5% of the total genes in the array. CPX also induces substantial mutation-dependent and -independent changes in **gene expression**. Some of these changes involve movement of **gene expression** in mutant cells in a direction resembling expression in wild-type cells. Conclusions: These data clearly demonstrate that cDNA array analysis of cystic fibrosis cells can yield useful pharmacogenomic information with significant relevance to both gene and pharmacological therapy. We suggest that this approach may provide a paradigm for genome-based surrogate endpoint **testing** of CF therapeutics prior to human administration.

Article title	Pharmacogenomics of the cystic fibrosis transmembrane conductance regulator (CFTR) and the cystic fibrosis drug CPX using genome microarray analysis
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Authors	Srivastava_M Eidelman_O Pollard_H_B
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or micro

L4 ANSWER 21 OF 25 MEDLINE
AN 94306657 MEDLINE
DN 94306657 PubMed ID: 8033337
TI Cardiomyocytes differentiated in vitro from **embryonic stem** cells developmentally express cardiac-specific genes and ionic currents.
AU Maltsev V A; Wobus A M; Rohwedel J; Bader M; Hescheler J
CS Institut fur Pflanzengenetik und Kulturpflanzenforschung, Gatersleben, Freie Universitat Berlin, Germany.
SO CIRCULATION RESEARCH, (1994 Aug) 75 (2) 233-44.
Journal code: DAJ; 0047103. ISSN: 0009-7330.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199408
ED Entered STN: 19940825
Last Updated on STN: 19940825
Entered Medline: 19940818
AB Cardiomyocytes differentiated in vitro from pluripotent **embryonic stem** (ES) cells of line D3 via embryo-like aggregates (embryoid bodies) were characterized by the whole-cell patch-clamp technique during the entire differentiation period. Spontaneously contracting cardiomyocytes were enzymatically isolated by collagenase from embryoid body outgrowths of early, intermediate, and terminal differentiation stages. The early differentiated cardiomyocytes exhibited an outwardly rectifying, transient K+ current sensitive to 4-aminopyridine and an inward Ca2+ current but no Na+ current. The Ca2+ current showed all features of L-type Ca2+ current, being highly sensitive to 1,4-dihydropyridines but not to omega-conotoxin. Cardiomyocytes of intermediate stage were characterized by the additional **expression** of cardiac-specific Na+ current, the delayed K+ current, and If current. Terminally differentiated cardiomyocytes expressed a Ca2+ channel density about three times higher than that of early stage. In addition, two types of inwardly rectifying K+ currents (IK1 and IK,Ach) and the ATP-modulated K+ current were found. During cardiomyocyte differentiation, several distinct cell populations could be distinguished by their sets of ionic channels and typical action potentials presumably representing cardiac tissues with properties of sinus node, atrium, and ventricle. Reverse transcription polymerase chain reaction revealed the transcription of alpha- and beta-cardiac myosin heavy chain (MHC) genes synchronously with the first spontaneous contractions. Transcription of embryonic skeletal MHC gene at intermediate and terminal differentiation stages correlated with the **expression** of Na+ channels. The selective **expression** of alpha-cardiac MHC gene in ES cell-derived cardiomyocytes was demonstrated after ES cell transfection of the LacZ construct driven by the alpha-cardiac MHC promoter region followed by ES cell differentiation and beta-galactosidase staining. In conclusion, our data demonstrate that ES cell-derived cardiomyocytes represent a unique model to investigate the early cardiac development and permit pharmacological/**toxicological** studies in vitro.

L14 ANSWER 2 OF 8 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 1999052885 EMBASE
TI Human **embryonic stem** cells: The future is now.
AU Keller G.; **Snodgrass H.R.**
CS G. Keller, Natl. Jewish Medical/Research Center, Denver, CO 80206, United States. kellorg@njc.org
SO Nature Medicine, (1999) 5/2 (151-152).
Refs: 15
ISSN: 1078-8956 CODEN: NAMEFI
CY United States
DT Journal; (Short Survey)
FS 029 Clinical Biochemistry
L